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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,675	05/27/2005	Akihiro Tada	TOYA107.006APC	9885

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EXAMINER

RAHMANI, NILOOFAR

ART UNIT PAPER NUMBER

1625

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/536,675	Applicant(s) TADA ET AL.	
	Examiner Niloofar Rahmani	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-11 are pending.

2. ***Priority***

This application is a 371 of PCT/JP03/15266, filed on 11/28/2003. The claimed benefit of priority date is denied. There is no certified translation of the priority document.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-6 are rejected because the term "a skin preparation" is confusing. Does it mean pharmaceutical composition or method for treating or method for using? Correction is required.

4. Claim 9 is rejected because the term "alleviating" is confusing. Correction is required.

5. Claim 7 is rejected because the term "comprising", on line 3 is confusing. Correction is required.

6. Claim 7 is rejected because the term "applying a skin preparation for external use" is confusing. To where is it applying a skin preparation? Does it apply to eye or skin or cell? Correction is required.

7. Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,

- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method for inhibiting elongation of melanocytic dendrites consisting of a compound of formula (I).

The state of the prior art: " Berberine, berberine derivatives and pharmaceutically acceptable salts thereof have a superior inhibitory effect on the elongation of melanocyte dendrites. Topical preparations for skin containing berberine, berberine derivatives and/or pharmacologically acceptable salts thereof have a preventative or ameliorative effect on dyschromia such as age spots due to exposure to light or injection." (JP 2001335485)

The state of the prior art is that it involves screening to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed

invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for inhibiting the elongation of melanocytic dendrites.

Amount of guidance/working examples: There is an example for inhibiting the elongation of human melanocytes by using compound methylophiopogonanone B. But applicant has not guidance or examples for inhibiting the elongation of melanocytic dendrites using the other compounds of claim 1. The specification does not seem to enable the correlation between the other compounds of claim 1 and the inhibiting the elongation of melanocytic dendrites.

The breadth of the claims: The breadth of claims is drawn to method for inhibiting elongation of melanocytic dendrites consisting of a compound of formula (I).

The quantity of experimentation needed: Since the guidance and teaching provided by the specification is insufficient for inhibiting the elongation of melanocytic dendrites, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 7-11, for method for inhibiting elongation of melanocytic dendrites, have been enabled by the instant specification.

8. *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by ZHU et al., Journal of Chromatography, vol.437, pages 265-267. ZHU et al. disclosed the instant claimed product on page 265, Fig 1, formula (B). Therefore, the instant claims are anticipated by ZHU et al.

9. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by KANEDA et al., Yakugaku Zasshi, vol.103, pages 1133-9. KANEDA et al. disclosed the instant claimed product on page 1134, formula methylophiopogonanone B(4). Therefore, the instant claims are anticipated by KANEDA et al.

10. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by TADA et al., Chemical & pharmaceutical Bulletin, vol.28, pages 1477-1484. TADA et al. disclosed the instant claimed product on page 1478, Chart I, formula

(IVa), where in $R_1=R'$ denotes Hydrogen group. Therefore, the instant claims are anticipated by TADA et al.

11. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by HUANG et al., *Phytochemistry*, vol.44, pages 1369-1373. HUANG et al. disclosed the instant claimed product on page 1371, formula 3, where in R_1-R_2 denotes methyl group and R_3 denotes Hydrogen group. Therefore, the instant claims are anticipated by HUANG et al.

12. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshiaki et al., *Chemical & Pharmaceutical Bulletin*, vol. 33, pages 5358-63. Yoshiaki et al. disclosed the instant claimed product on page 5361, Chart 1, formula 4, wherein R being CH_3 and formula 9, 10, where in R being CH_3 and H. Therefore, the instant claims are anticipated by Yoshiaki et al.

13. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Takatsuki et al., *Natural Medicines*, vol. 52, pages 145-150. Takatsuki et al. disclosed the instant claimed product on page 148 Chart 1, methylophiopogonanone B (2). Therefore, the instant claims are anticipated by Takatsuki et al.

14. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Watanabe et al., *Shoyakugaku Zasshi*, vol. 44, pages 117-21. Watanabe et al. disclosed the instant claimed product on page 118, Fig 1, SE-5, wherein R_1 being CH_3 , R_2 and R_3 being H, R_4 being OCH_3 . Therefore, the instant claims are anticipated by Watanabe et al.

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15. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al., Yaoxue Xue Bao, vol. 22, pages 679-84. Zhu et al. disclosed the instant claimed product on page 630, Fig 2, formula II. Therefore, the instant claims are anticipated by Zhu et al.

16. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by ROSEN et al., WO 01/56580. ROSEN et al. disclosed the instant claimed product on page 4, Formula (II). Therefore, the instant claims are anticipated by ROSEN et al.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI

03/14/2006

NA


D. MARGARET SEAMAN

PRIMARY EXAMINER

GROUP 1625